II. REMARKS:

A. Status of the Claims

Claims 1 and 2 were originally filed with the case. Both claims were rejected in an Office Action mailed on May 30, 2006. Claim 1 was amended, claim 2 was canceled, and claims 3-18 were added in a Response to Office Action filed on October 30, 2006. All claims are rejected in the Final Office Action mailed on January 12, 2007. Claims 1, 7, 9, 11, 13 and 16 are amended herein, claims 14 and 15 are cancelled herein and no claims are added herein. Support for the amendments to claim 1 can be found in the specification, particularly at page 3, line 37 to page 4, line 2. Support for the amendments to claim 13 can be found Example 5 on page 9. Claims 7, 9, 11, and 16 were amended to correct the dependencies. Thus, claims 1, 3-13, and 16-18 are pending.

B. Terminal Disclaimer Establishes the Patentability of the Claims Over Co-pending Application No. 10/772,963

The Action rejects claims 1 and 3-18 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3-18 of co-pending application no. 10/772,963 in view of Penn *et al.* The '963 application is directed to the treatment of pathologic ocular angiogenesis and associated edema by administration of compositions containing a glucocorticoid and anecortave acetate. Penn is said to show that diabetic retinopathy is an angiogenic ocular condition. Applicants respectfully traverse.

The posterior segment neovascularization (PSNV) found in exudative AMD is characterized as pathologic choroidal NV, whereas proliferative diabetic retinopathy (PDR)

exhibits preretinal NV. Pathologic ocular angiogenesis, which includes PSNV, occurs as a cascade of events that progress from an initiating stimulus to the formation of abnormal new capillaries. Treatments for PSNV and PDR differ. Approved treatments for the PSNV in exudative AMD include laser photocoagulation and photodynamic therapy with Visudyne®; both therapies involve laser-induced occlusion of affected vasculature and are associated with localized laser-induced damage to the retina. For patients with PDR, grid or panretinal laser photocoagulation and surgical interventions, such as vitrectomy and removal of preretinal membranes, are the only options currently available. Thus, it is submitted that treatments for diabetic retinopathy will not necessarily be effective for treating all pathologic ocular angiogenesis in general.

Nevertheless, Applicants submit herewith a terminal disclaimer over the '963 application in order to move the present case toward allowance. Therefore, Applicants respectfully request that the double-patenting rejection based on co-pending application 10/772,963 be withdrawn.

C. <u>The Claims are Not Obvious</u>

The Action sets forth a number of obviousness rejections, each of which is addressed separately hereunder.

1. ***The Claims are Patentable Over Penn in view of Jonas***

The Action rejects claims 1, 3-6 and 13-16 as being unpatentable over Penn in view of Jonas. Penn is said to teach the use of angiostatic steroids, particularly anecortave acetate, to treat angiogenic ocular conditions, including diabetic retinopathy. Penn is said to show the

use of a 10% suspension of anecortave acetate. Jonas is said to teach the use of cortisone to treat nonproliferative diabetic retinopathy. The Action acknowledges that neither Penn nor Jonas expressly teaches that the combination of a glucocorticoid and anecortave acetate is useful in a method to treat diabetic retinopathy or retinal edema. Nevertheless, the Action asserts that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a glucocorticoid in combination with anecortave acetate for the treatment of nonproliferative diabetic retinopathy "to optimize the effective amounts of active agents in the composition to be administered." Applicants respectfully traverse.

The present invention is directed to a method for treating a person suffering from retinal edema or nonproliferative diabetic retinopathy by administering a preservative-free composition containing a glucocorticoid and anecortave acetate. Neither Penn nor Jonas discusses preservative-free compositions. The Action asserts that neither Jonas nor Penn discusses the use of any classical preservatives, therefore the skilled artisan would not consider the use of classical preservatives a necessity. Neither Penn nor Jonas discusses the components of the compositions used in their studies at all. At the time Penn performed his study with anecortave acetate, that compound was being studied in clinical trials for the treatment of AMD. A 3% suspension, containing the preservative benzalkonium chloride (see U.S. Patent No. 5,679,666, Example 1) was one of the compositions studied in the trials. Furthermore, Jonas describes the intravitreal injection of crystalline cortisone (20 mg triamcinolone acetonide), which remains intravitreally for up to 3 months after injection. Jonas does not discuss the administration of a composition containing a glucocorticoid at all.

According to the Supreme Court's recent decision in *KSR International Co. v. Telefax Inc. et al.*, 550 U.S. (2007), a finding of obviousness still requires a showing that there was a reason to combine the elements of cited references. The May 3, 2007, memorandum to the patent examining corps further emphasized that the PTO examiner must "identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed."

The Final Action has failed to provide a reason for the skilled artisan to combine the teachings of the cited references to arrive at a method of treating a person suffering from retinal edema or non-proliferative diabetic retinopathy by administering a preservative-free composition containing both a glucocorticoid and anecortave acetate.

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection based on Penn and Jonas be withdrawn.

2. *The claims are Patentable over Penn in view of Guo*

Next, the Action rejects claims 1, 3-6, 9-16, and 18 as being unpatentable over Penn in view of Guo further in view of the Merck Manual. Penn is said to disclose the use of angiostatic steroids, particularly anecortave acetate, to treat angiogenic ocular conditions, including diabetic retinopathy and to show the use of a 10% suspension of anecortave acetate. Guo is said to disclose the use of corticosteroids for the treatment of diseases of the retina, including ocular inflammation, diabetic macular edema, cystoid macular edema and macular edema. Guo is further said to disclose a method for delivering a corticosteroid by implanting a sustained release device. The Merck Manual is said to teach that edema is one of the symptoms of

nonproliferative retinopathy. The Action argues that it would have been obvious to the skilled artisan to employ a glucocorticoid in combination with anecortave acetate because the compounds were known to be useful for the same purpose. Applicants respectfully traverse.

The present invention is directed to a method for treating a person suffering from retinal edema or non-proliferative diabetic retinopathy by administering a preservative-free composition containing both a glucocorticoid and anecortave acetate. As stated above, although Penn does not discuss the particular components of the composition studied, it is likely that the composition used contained preservatives in light of the compositions of anecortave acetate being studied in clinical trials for the treatment of AMD at that time. As acknowledged in the Action, Guo discussed the administration of a sustained release device containing a corticosteroid to the vitreous of an eye to treat diseases of the retina. Guo defines a "sustained release device" as a device that releases drug over an extended period of time in a controlled fashion." (Column 2, lines 57-59). In short, Guo does not discuss administration of a composition containing a glucocorticoid, much less a preservative-free composition containing a glucocorticoid.

Applicants fail to understand the reason a skilled artisan would find it obvious to combine a teaching of a sustained release device containing a glucocorticoid with a composition containing anecortave acetate and at least one preservative to arrive at a preservative-free composition containing both a glucocorticoid and anecortave acetate for the treatment of retinal edema or non-proliferative diabetic retinopathy. Applicants therefore respectfully request that such a reason be provided, or the rejection based on Penn in view of Guo in further view of The Merck Manual be withdrawn.

3. *The Claims are Patentable over Penn in view of Drugs & Therapy Perspectives*

Claims 1, 3-4, and 7-10 are rejected as being unpatentable over Penn in view of Drugs & Therapy Perspectives further in view of the Merck Manual. Penn and the Merck Manual are cited for the disclosures set forth above. Drugs & Therapy Perspectives is said to disclose that rimexolone is effective against ocular inflammation (edema). Again, the Action asserts that the skilled artisan would have found the claimed invention obvious because both rimexolone and anecortave acetate were known to be useful for the same purpose. Applicants respectfully traverse.

Contrary to the Action's assertion, Drugs & Therapy Perspectives does not teach the use of rimexolone to treat retinal edema or non-proliferative diabetic retinopathy. Rather, Drugs & Therapy Perspectives appears to disclose only the topical administration of a 1% ophthalmic suspension containing rimexolone for the treatment of anterior uveitis and for controlling ocular inflammation after cataract surgery. It is submitted that ocular inflammation resulting from cataract surgery (a surgery affecting the tissues at the front of the eye) is not the same as retinal edema (a condition affecting the tissues at the back of the eye).

The present invention is directed to a method of treating retinal edema or non-proliferative diabetic retinopathy by administering a preservative-free composition containing a glucocorticoid and anecortave acetate. Drugs & Therapy Perspectives does not discuss the components of the ophthalmic suspension applied topically for the treatment of uveitis or ocular inflammation resulting from cataract surgery. However, Vexol®, the 1% rimexolone ophthalmic suspension typically used in such studies, contains the preservative benzalkonium chloride (see

http://www.rxlist.com/cgi/generic/rimexol.htm.). As stated above, the anecortave acetate composition used by Penn in his studies also likely contained the preservative, benzalkonium chloride. Therefore, Applicants can find no reason the skilled artisan would combine the teachings of the cited references to make a preservative-free composition containing a glucocorticoid and anecortave acetate to be used for the treatment of retinal edema or non-proliferative diabetic retinopathy.

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection based on Penn in view of Drugs & Therapy Perspectives in further view of the Merck Manual be withdrawn.

4. *The Claims are Patentable over Penn in view of Clark*

Finally, the Action rejects claims 1 and 17 as being unpatentable over Penn in view of Clark. Penn is cited for the teachings discussed above. Clark is said to disclose a method for sub-Tenon delivery of drug depot, in particular anecortave acetate, to the posterior segment of the eye. Clark is further said to disclose the method for delivery of steroidal anti-inflammatory agents. The Action asserts that glucocorticoids are steroidal anti-inflammatory agents. The Action argues that the skilled artisan would reasonably expect that the use of posterior juxtascleral injection of a combination of a glucocorticoid with anecortave acetate would improve the therapeutic effects for treating non-proliferative diabetic retinopathy because anecortave acetate is known for its effectiveness against diabetic retinopathy and glucocorticoids are known for their effectiveness against retinal edema. Applicants respectfully traverse.

Applicants reiterate that the present invention is directed to a method for treating a person suffering from retinal edema or non-proliferative diabetic retinopathy by administering a preservative-free composition containing both a glucocorticoid and anecortave acetate. It is likely that Penn administered an anecortave acetate composition containing anecortave acetate in the performance of his studies. Clark is directed to a drug delivery device useful for administering compositions via sub-Tenon drug delivery to the posterior segment of the human eye proximate to the macula. Clark provides a long list of a number of compounds, or types of compounds, which might be successfully delivered via the described device. When discussing anecortave acetate, Clark points to U.S. Patent No. 5,679,666. This patent discloses only compositions of anecortave acetate containing preservatives, such as benzalkonium chloride. Although Clark also suggests that steroidal anti-inflammatory agents may be delivered via the disclosed device, it does not suggest any particular glucocorticoid agents, nor does it suggest administering a combination of glucocorticoids with anecortave acetate.

Again, Applicants fail to find a reason the skilled artisan would have combined the teachings of Penn and Clark to produce a preservative-free composition containing a glucocorticoid and anecortave acetate useful for treating retinal edema or non-proliferative diabetic retinopathy.

In light of the foregoing comments, Applicants respectfully request that the obviousness rejection based on Penn in view of Clark be withdrawn.

D. Conclusion

This is submitted to be a complete response to the outstanding Action. Based on the foregoing arguments, the claims are believed to be in condition for allowance; a notice of allowability is therefore respectfully requested.

The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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